

U.S.S.N. 09/848,664
Filed: May 3, 2001
AMENDMENT AND RESPONSE TO OFFICE ACTION

Amendment to the Claims

1. (Currently Amended Twice) A drug delivery composition comprising:

a) a substrate;

b) a bi-domain peptide comprising a first domain that binds heparin or heparin-like compounds with high affinity and a second domain that binds to the substrate,

wherein the second domain ~~peptide~~ is covalently bound to the substrate so that the ~~heparin-binding~~ first domain is able to bind to heparin or heparin-like compounds;

c) heparin or a heparin-like polymer; and

d) a protein growth factor or a peptide fragment thereof having a domain that binds heparin with low affinity, wherein the protein growth factor or the peptide fragment thereof binds with low affinity to the heparin or heparin-like polymer of (c), and wherein low affinity is defined as not binding with heparin at a NaCl concentration of between about 25 mM and 140 mM.

Claim 2 (Previously canceled).

~~2.~~ (Previously Amended) The composition of claim 1 wherein the domain of the growth factor or peptide fragment thereof is further defined as comprising a length of about 8 to 30 amino acid residues comprising at least 2 basic amino acid residues, a ratio of basic to acidic amino acid residues of at least 2, and a ratio of hydrophobic amino acid residues to basic amino acid residues of at least 0.67.

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~~3~~². (Previously Amended) The composition of claim ~~1~~² wherein the basic amino acid residues are K or R.

~~4~~². (Previously Amended) The composition of claim ~~6~~² wherein the acidic amino acid residues are further defined as D or E.

~~5~~². (Previously Amended) The composition of claim ~~7~~² wherein the hydrophobic amino acid residues are further defined as A, V, F, P, M, I, or L or C when C is involved in a disulfide bond.

~~6~~². (Previously Amended) The composition of claim ~~7~~² wherein the growth factor or peptide fragment thereof is selected from the group consisting of neurturin, persephin, IGF-1A, IGF-1 β , EGF, NGF β , NT-3, BDNF, NT-4, TGF- β 3, and TGF- β 4.

Claims 8-19 (Previously Canceled).

~~14~~¹³. (Previously Amended) The composition of claim ~~65~~¹³ wherein the substrate comprises fibrin.

~~15~~¹³. (Previously Amended) The composition of claim ~~65~~¹³ wherein the substrate comprises a synthetic polymer hydrogel.

Claims 22 and 23 (Previously Canceled).

~~16~~¹². (Previously Amended) The composition of claim ~~64~~¹² wherein the heparin or heparin-like polymer has a molecular weight between about 3,000 and 10,000,000 Daltons.

~~17~~¹³. (Previously Amended) The composition of claim ~~64~~¹³ wherein the heparin-like polymer is a polysaccharide having a molecular weight between about 3,000 and 10,000,000

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Daltons, and having at least one negative charge per two saccharide rings and no more than one positive charge per ten saccharide rings.

~~18~~ ¹² (Currently Amended Twice) The composition of claim ~~64~~ wherein the heparin-like polymer is selected from the group consisting of dextran ~~sulfate~~ sulfates, chondroitin ~~sulfate~~ sulfates, heparin ~~sulfate~~ sulfates, fucan ~~fucans~~, ~~alginate and alginates~~, and a derivative thereof.

~~7~~ (Previously Amended) The composition of claim 1 wherein the molar ratio of heparin or heparin-like polymer to growth factor or peptide fragment thereof is at least one.

Claims 28-56 (Previously Canceled).

~~8~~ (Previously Amended) The composition of claim 1 in a vascular graft.

~~9~~ (Previously Amended) The composition of claim 1 in an article for treatment of dermal wounds.

~~10~~ ⁹ (Previously Amended) The composition of claim ~~58~~, wherein the growth factor is TGF- β 3.

Claim 60 (Previously Canceled).

~~11~~ (Previously Amended) The composition of claim 1 in an implantable sterilized composition.

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19 ~~2~~. (Currently Amended Twice) A method for providing controlled release of a growth factor comprising:

preparing a composition comprising

a) a substrate,

b) a bi-domain peptide comprising a first domain that binds heparin or heparin-like compounds with high affinity and a second domain that binds to the substrate, wherein the second domain peptide is covalently bound to the substrate so that the heparin-binding first domain is able to bind to heparin or heparin-like compounds,

c) heparin or a heparin-like polymer, and

d) a growth factor or a peptide fragment thereof having a domain with low affinity for binding heparin and bound heparin or heparin-like polymer, wherein the protein growth factor or the peptide fragment thereof binds with low affinity to the heparin or heparin-like polymer of (c), and wherein low affinity is defined as not binding with heparin at a NaCl concentration of between about 25 mM and 140 mM; and placing the composition on a wound in need thereof.

20 ~~3~~. (Previously Amended) The method of claim 62, wherein the growth factor or a peptide fragment thereof is released by dissociation of the growth factor from the heparin or heparin-like polymer.

12 ~~4~~. (Previously Added) The composition of Claim 1, wherein the heparin or heparin-like compound is non-covalently attached to the peptide.

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13/ (Previously Added) The composition of Claim 1 wherein the substrate is selected from the group comprising fibrin, collagen and synthetic polymer hydrogels.

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